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Amendments to the Claims

Claim 1 (currently amended): A modified molecule having the biological activity of human erythropoietin (EPO) and being substantially non-immunogenic or less immunogenic than any non-modified molecule having the same biological activity in an individual when used *in vivo*, wherein (i) the said loss of immunogenicity is achieved by removing one or more T-cell epitopes derived from the originally non-modified molecule and said T-cell epitopes are MHC class II ligands or peptide sequences which show the ability to stimulate or bind T-cells via presentation on class II,

(ii) said modified molecule, when tested as a whole protein in a biological human T-cell proliferation assay, exhibits a stimulation index (SI) smaller than the parental non-modified molecule and smaller than 2.0, and

(iii) said T-cell epitopes to be removed are located on strings of contiguous residues of the originally non-modified EPO molecule, the strings are selected from:

(a) RVLERYLLEAKEAENITTGCAEHCSLNENITVP (SEQ ID NO: 2; residues 10-42 of SEQ ID NO: 1), wherein the at least one amino acid residue substitution in epitope region (a) is selected from the group consisting of Ile25Ala, Ile25Gly, Ile25Pro, Leu35Ala, Leu35Asp, Leu35Glu, Leu35Gly, Leu35His, Leu35Lys, Leu35Asn, Leu35Pro, Leu35Gln, Leu35Arg, Leu35Ser, and Leu35Thr;

(b) RGQALLVNSSQPWEPLQLHVDKAVSGLRSLTTL (SEQ ID NO: 3; residues 76-108 of SEQ ID NO: 1), wherein the at least one amino acid residue substitution in epitope region (b) is selected from the group consisting of Trp88Thr, Trp88Ala, Trp88Gly, Leu91Ala, Leu91Asp, Leu91Glu, Leu91Gly, Leu91His, Leu91Lys, Leu91Asn, Leu91Pro, Leu91Gln, Leu91Arg, Ser, Leu91Thr, Leu93Ala, Leu93Asp, Leu93Glu, Leu93Gly, Leu93His, Leu93Lys, Leu93Asn, Leu93Pro, Leu93Gln, Leu93Arg, Leu93Ser, Leu93Thr, Val95Ala, Val95Asp, Val95Glu, Val95Gly, Val95His, Val95Lys, Val95Asn, Val95Pro, Val95Gln, Val95Arg, Val95Ser, and Val95Thr; and

(c) RTITADTFRKLFRVYSNFLRGKLKLYTGEACRT (SEQ ID NO: 4; residues 131-163 of SEQ ID NO: 1), wherein the at least one amino acid residue substitution in epitope region (c) is selected from the group consisting of: Ile141Thr, Phe142Ala, Phe142Gly, Phe142Pro, Val144Thr, Tyr145Ala, Tyr145Gly, Tyr145Pro, Phe148Ala, Phe148Gly, Phe148Pro, Leu149Ala, Leu149Asp, Leu149Gly, Leu149His, Leu149Lys,

Leu149Asn, Leu149Pro, Leu149Gln, Leu149Arg, Leu149Ser, Leu149Thr, Leu153Ala, Leu153Asp, Leu153Glu, Leu153Gly, Leu153His, Leu153Lys, Leu153Asn, Leu153Pro, Leu153Gln, Leu153Arg, Leu153Ser, and Leu153Thr.

Claims 2-20 (canceled).

Claim 21 (currently amended): An isolated polypeptide having the biological activity of native human erythropoietin and being less immunogenic to a human than native human erythropoietin, the polypeptide comprising the amino acid residue sequence of SEQ ID NO: 1 and including at least one amino acid residue substitution ~~in at least one epitope region of SEQ ID NO: 1 selected from the group consisting of (a) amino acid residues 10-42 of SEQ ID NO: 1, (b) amino acid residues 76-108 of SEQ ID NO: 1, and (c) amino acid residues 131-163 of SEQ ID NO: 1~~ selected from the group consisting of Ile25Ala, Ile25Gly, Ile25Pro, Leu35Ala, Leu35Asp, Leu35Glu, Leu35Gly, Leu35His, Leu35Lys, Leu35Asn, Leu35Pro, Leu35Gln, Leu35Arg, Leu35Ser, Leu35Thr, Trp88Thr, Trp88Ala, Trp88Gly, Leu91Ala, Leu91Asp, Leu91Glu, Leu91Gly, Leu91His, Leu91Lys, Leu91Asn, Leu91Pro, Leu91Gln, Leu91Arg, Ser. Leu91Thr, Leu93Ala, Leu93Asp, Leu93Glu, Leu93Gly, Leu93His, Leu93Lys, Leu93Asn, Leu93Pro, Leu93Gln, Leu93Arg, Leu93Ser, Leu93Thr, Val95Ala, Val95Asp, Val95Glu, Val95Gly, Val95His, Val95Lys, Val95Asn, Val95Pro, Val95Gln, Val95Arg, Val95Ser, Val95Thr, Ile141Thr, Phe142Ala, Phe142Gly, Phe142Pro, Val144Thr, Tyr145Ala, Tyr145Gly, Tyr145Pro, Phe148Ala, Phe148Gly, Phe148Pro, Leu149Ala, Leu149Asp, Leu149Gly, Leu149His, Leu149Lys, Leu149Asn, Leu149Pro, Leu149Gln, Leu149Arg, Leu149Ser, Leu149Thr, Leu153Ala, Leu153Asp, Leu153Glu, Leu153Gly, Leu153His, Leu153Lys, Leu153Asn, Leu153Pro, Leu153Gln, Leu153Arg, Leu153Ser, and Leu153Thr.

Claims 22-29 (canceled).

Claim 30 (previously presented): An isolated nucleic acid that encodes a polypeptide of claim 21.

Claims 31 and 32 (canceled).

Claim 33 (previously presented): A pharmaceutical composition comprising a polypeptide of claim 21 in a pharmaceutically acceptable carrier therefor.

Claims 34 and 35 (canceled).

Claim 36 (previously presented): The isolated polypeptide of claim 21 wherein the polypeptide exhibits a stimulation index of less than 2 when tested in a biological human T-cell proliferation assay.

Claim 37 (previously presented): The isolated polypeptide of claim 21 wherein the polypeptide exhibits a stimulation index of less than 1.8 when tested in a biological human T-cell proliferation assay.

Claim 38 (currently amended): The isolated polypeptide of claim 21 wherein the at least one amino acid residue substitution ~~in epitope region (c)~~ is Phe142Ala or Val144Thr or Tyr145Pro.

Claim 39 (new): An isolated polypeptide comprising the amino acid residue sequence of SEQ ID NO: 1 including at least one amino acid residue substitution selected from the group consisting of Phe142Ala, Val144Thr, and Tyr145Pro.

Claim 40 (new): A pharmaceutical composition comprising a polypeptide of claim 38 in a pharmaceutically acceptable carrier therefor.

Claim 41 (new): A pharmaceutical composition comprising a polypeptide of claim 39 in a pharmaceutically acceptable carrier therefor.

Claim 42 (new): An isolated nucleic acid that encodes a polypeptide of claim 38.

Claim 43 (new): An isolated nucleic acid that encodes a polypeptide of claim 39.